Concurrent lymphoma and salmonellosis in a cat

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Salmonella spp. have been isolated from the feces of asymptomatic cats purchased for use in research, with varying prevalence according to the source of the cat (1). Clinical signs attributable to *Salmonella* infection have been infrequently reported (2,3), but hematochezia or diarrhea, vomiting, fever with leukopenia, and hepatic dysfunction have all been reported in cats with *Salmonella*-containing feces (2,3). Cultures of wounds or blood may also yield *Salmonella* spp. It is presumed, but not proven, that stress and immunosuppression caused by agents such as the feline leukemia virus (FeLV), play a role in the pathogenesis of feline salmonellosis. Our purpose in this report is to describe a case of feline lymphoma complicated by *Salmonella* septicemia.

A 15-year-old, neutered male, domestic shorthair cat weighing 3 kg was examined because of polyuria, polydipsia, and weight loss of one month's duration. On examination, the cat was thin and icteric. Abdominal palpation indicated diffuse abdominal pain, hepatomegaly, and irregularly-shaped kidneys. A tentative diagnosis of hepatic or renal disease was made and diagnostic testing was initiated.

A complete blood count (CBC), metabolic profile, coagulogram, and urinalysis were performed (Table 1, January 10). Mild neutrophilia, lymphopenia, and eosinophilia were noted on the CBC. Biochemical abnormalities included hyperbilirubinemia and high liver enzymes. Urinalysis revealed 3+ bile and a specific gravity of 1.012. The coagulogram revealed thrombocytopena and prolonged prothrombin (PT) and partial thromboplastin (PTT) times. Hepatomegaly was the only abnormality noted on abdominal radiography. Feline leukemia virus and feline immunodeficiency virus ELISA tests were both negative. The resting T_4 value was normal (30.8 nmol/L; normal value, 10–50 nmol/L).

In view of the clinical and laboratory abnormalities, a diagnosis was made of vitamin K deficiency coagulopathy secondary to hepatopathy of unknown cause. An intravenous catheter was inserted and treatment initiated with lactated Ringer's solution (20 mL/kg, q8h, IV), a multiple vitamin B supplement (0.5 mL, q8h, IV), chloramphenicol (10 mg/kg, q12h, PO), and vitamin K1 (5 mg, q12h, SC). A repeat coagulogram (January 12) revealed improvement in the PT and PTT times. Persistent abnormality in the PTT was probably caused by the inability of the diseased liver to adequately activate or produce clotting factors. Repeat biochemical analysis (January 12) revealed no remarkable change from the results of previous testing.

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Exploratory laparotomy on day 5 of hospitalization revealed a yellow, rounded liver and diffusely thickened intestines. Biopsy specimens of the liver, mesenteric lymph node, and small intestine were submitted for histological examination. The treatment that was initiated before surgery was continued.

Two days after surgery, the cat was febrile (40.3°C), and began vomiting and passing liquid, brown stool. Fluid was palpated in the abdomen. Repeat hematological testing (January 17) revealed neutrophilia, lymphopenia, and eosinophilia with a left shift and anemia. Biochemical analysis (January 17) revealed that there had been no change in the bilirubin, but the liver enzymes were less elevated. Because of the abnormal hematological findings, we suspected septicemia from surgical cotamination or wound dehiscence, or progression of the underlying disease. Abdominocentesis performed 2 d after surgery yielded several milliliters of icteric, cloudy fluid which was submitted for bacterial culture and cytological testing; the latter revealed mild peritonitis without bacteria. A fecal specimen was also submitted for bacterial culture. Blood was not submitted for culture because of the large volume of blood required and the small size and anemic status of the cat.

In view of the clinical and laboratory abnormalities, a diagnosis was made of vitamin K deficiency coagulopathy secondary to hepatopathy of unknown cause

Empiric treatment of sepsis was initiated by administration of netilmycin sulfate (Netromycin, Schering Corporation, Kenilworth, New Jersey) (0.5 mg/kg, q8h, IV) and ticarcillin disodium (Ticar, Beecham Laboratories Inc., Bristol, Tennessee) (30 mg/kg, q8h, IV). The dosage of fluid administration was increased (30 mL/kg, q8h, IV) to make up for additional fluid losses from vomiting and diarrhea. The pyrexia resolved on the third postoperative day, but the vomiting and diarrhea continued. The left shift and icterus also persisted (January 18).

The histopathology report received 3 d postoperatively was consistent with lymphoma in all organs biopsied. Chemotherapy was initiated on the seventh postoperative day by administration of L-asparaginase (Elspar, Merck, Sharpe and Dohme, West Point, Virginia) (400 IU/kg, IP), vincristine (0.025 mg/kg, IV) and prednisone (5 mg, q12h, PO) in the hope that the clinical status of the cat would improve by treatment of the underlying neoplasia.

The cat's condition continued to deteriorate, and, on the eighth postoperative day, *Salmonella typhimurium* was isolated from the feces and abdominal fluid. The organism was sensitive to both netilmycin and ticarcillin, but only mildly sensitive to

Table 1. Selected laboratory data from a cat with concurrent lymphoma and salmonellosis

	Reference values	Jan 10	Jan 12	Jan 17	Jan 18	Jan 22
WBC ($\times 10^9$/L)	6–13.5	6.9	—	13.0	12.7	7.9
Monocytes ($\times 10^9$/L)	0.12–0.81	0.7	—	0.0	0.6	0.0
Lymphocytes ($\times 10^9$/L)	1.1–8.4	0.8	—	0.6	1.0	0.4
Neutrophils ($\times 10^9$/L)	3.0–10.1	5.5	—	10.7[a]	10.0[a]	6.7
Bands ($\times 10^9$/L)	0–0.4	0.0	—	1.4	1.0	0.8
Eosinophils ($\times 10^9$/L)	0.1–0.7	0.5	—	2.6	0.0	0.0
PCV (L/L)	0.27–0.40	39	—	24	18	18
Total bilirubin (μmol/L)	1.7–10.3	84	96	100	113	147
SAP (U/L)	10–400	2390	2000	200	390	200
ALT (U/L)	50–750	3810	3130	1040	1010	390
AST (U/L)	50–600	1440	1620	1340	550	880
Platelets ($\times 10^9$/L)	300–600	64	260	—	—	—
PT (s)	10.3	11.8	10.3	—	—	—
PTT (s)	15.5	27.2	20.8	—	—	—

[a]Toxic change

chloramphenicol. Combination antibiotic therapy was continued. On the ninth postoperative day (January 22), the cat had a persistent left shift and remained icteric. It died on the tenth postoperative day.

On necropsy, the liver was moderately large and characterized by pallor and marked, random, disseminated, punctate, 2 to 3 mm white foci. There was marked diffuse thickening of the small intestine and dilation of the colon. The colon had irregular mucosal thickening due to adherent flocculent material. The lungs were mottled tan brown and had focal firm areas that were purple. A large amount of light serosanguinous exudate was seen in the thoracic and abdominal cavities.

On histopathological examination, the liver was found to have marked, diffuse portal infiltrates composed predominantly of moderately pleomorphic lymphocytes and lesser numbers of neutrophils. There was marked diffuse hypertrophy of Kupffer cells, and many were packed with rod-shaped, 1 to 2 μm, basophilic organisms interpreted as bacteria. Occasional macrophages within the pulmonary alveolar septa had cytoplasm packed with organisms as described for the liver. Intravascular colonies of bacteria were also found in small venules within the lung. The small intestines had erosions, ulcerations, and loss of most villi and crypts. There was a marked, diffuse infiltrate in the mucosa and submucosa composed of a mixed population of cells including macrophages, neutrophils, and a few lymphocytes. Occasional macrophages in the submucosa contained intracellular bacteria. *Salmonella typhimurium* was cultured from the spleen, liver, intestine, and bone marrow. The final diagnosis was hepatic lymphosarcoma and acute, multifocal, random, necrotizing hepatitis with intracellular bacteria, interstitial pneumonia with intravascular bacteria, and ulcerative enterocolitis with intracellular bacteria.

In man and dogs, salmonellosis is associated with immunosuppression caused by neoplasia and chemotherapy, hospitalization, and oral antibiotic therapy (4–6). Previous reports of feline salmonellosis have implicated hospitalization, surgical stress, and immunosuppression by FeLV or diabetes mellitus in the pathogenesis of the disease, but not neoplasia or chemotherapy (2,3). Salmonellosis was not reported as a complication of chemotherapy in a large group of cats with lymphoma (7).

Several potential mechanisms of *Salmonella* infection and dissemination, either alone or in combination, can be hypothesized in this case. In one study, 10.6% of random source cats were positive for *Salmonella* spp. (8). This cat could have become contaminated at surgery by its own endogenous bacteria. A nosocomial infection from a contaminated dish, thermometer, or cage of an asymptomatic or convalescent carrier cat shedding bacteria fecally, orally, or conjunctivally during hospitalization was also a consideration.

The final diagnosis was hepatic lymphosarcoma and acute, multifocal, random, necrotizing hepatitis with intracellular bacteria, interstitial pneumonia with intravascular bacteria, and ulcerative enterocolitis with intracellular bacteria

Disruption of the normal intestinal barrier by neoplastic infiltration might have allowed vascular invasion by the pathogen. Immunosuppression by chemotherapeutic agents and glucocorticoids might have led to subsequent dissemination of the bacteria.

T-cell dependent macrophage activation has been shown to be important for the survival of mice infected with *Salmonella* spp. (9). Dogs with lymphoma have been shown to have decreased cell-mediated immunity, and the same could be supposed for cats with lymphoma (10). A similar defect in this cat would have decreased normal bactericidal mechanisms, predisposing the cat to sepsis.

Preoperative preparation with oral antibiotics with a spectrum of activity including enteric organisms may have allowed the proliferation of a pathogenic strain

of *Salmonella*, or induced antibiotic resistance of the organism, predisposing the patient to overwhelming sepsis. *Salmonella* spp. are generally believed to be sensitive to chloramphenicol, but, in this cat, the pathogen was only mildly sensitive to chloramphenicol, perhaps because the animal had been treated with oral chloramphenicol on admission to the hospital. The role of hospitalization and surgery as stressful events cannot be ignored.

Diarrhea, vomiting, and fever, typical in feline salmonellosis, were seen in this cat. Leukopenia is common in cats with salmonellosis as it often is in dogs, horses, and man (2). In contrast, this cat initially had mild leukocytosis and a left shift which progressed to a severe left shift. The septic abdominal effusion in this case was also an unusual finding. Pathological findings at necropsy confirmed the clinical diagnosis of *Salmonella* septicemia.

In conclusion, salmonellosis should be considered as a potential complication of feline lymphoma in the presence of signs consistent with acute sepsis, although cats with lymphoma not complicated by salmonellosis may have similar clinical signs. If salmonellosis is suspected, appropriate bacterial cultures should be obtained and empiric treatment of sepsis initiated. Bacterial culturing of fecal material before initiation of chemotherapy may be indicated in order to identify cats at risk of developing salmonellosis and to warn their owners of the zoonotic potential.

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